

# Fragmentation Mechanism of *Trans*- $\alpha$ -Aryl- $\beta$ -enamino Esters

JIANG, Nan(蒋楠)    WANG, Jian-Bo(王剑波)    HE, Mei-Yu\*(何美玉)

College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, China

Electron impact-induced fragmentation mechanisms of *trans*- $\alpha$ -aryl- $\beta$ -enamino esters were investigated using mass-analyzed ion kinetic energy (MIKE) spectrometry and high resolution accurate mass data. It was found that the main characteristic fragmentations of compounds studied were: an odd electron ion  $M^{\ddagger} - EtOH$  was formed by losing a neutral molecule of ethanol; and the skeletal rearrangements took place; and the ring opening reaction happened after losing a carbon monoxide; and the typical McLafferty rearrangement underwent in ester group. The cyclization reaction caused by losing neutral molecule of  $TsNH_2$  due to the *ortho*-effects of substituted group of aromatic ring was also observed.

**Keywords**  $\alpha$ -aryl- $\beta$ -enamino esters, mechanism, MIKES, skeletal rearrangement, cyclization reaction

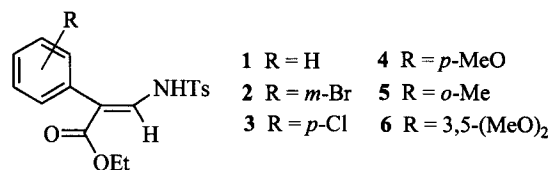
## Introduction

Diazocarbonyl compounds can be decomposed by transition metal complexes to generate metal carbenes, which can subsequently undergo diverse chemical transformations, including cyclopropanation, X—H insertion and ylide formation.<sup>1</sup> In addition, Diazocarbonyl compounds can give rise to rearrangement reactions, including Wolff rearrangement,<sup>2</sup> 1, 2-hydride<sup>3</sup> or 1, 2-alkyl migration.<sup>4</sup> Recently, we have successfully developed a new method to prepare  $\alpha$ -diazocarbonyl esters bearing an *N*-tosyl protected amino group. These newly formed diazo compounds were subjected to the catalytic decomposition with  $Rh_2(OAc)_4$ . It is observed that the neighboring aromatic ring migrates to the carbon center of the diazo carbon.<sup>5</sup> This novel rearrangement provides an efficient route to the  $\alpha$ -aryl- $\beta$ -enamino esters, which could be served as precursors for the synthesis of  $\alpha$ -substituted  $\beta$ -amino

acids.<sup>6</sup>

In the course of this investigation, a series of  $\alpha$ -aryl- $\beta$ -enamino esters were obtained. All these six compounds have not been reported in the literature to our knowledge. Their structures have been fully characterized using elemental analysis, MS, IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra (Scheme 1).

Schemes 1 Structures of compounds 1—6



Their fragmentation mechanisms were investigated in detail under electron impact (EI) conditions using mass-analyzed ion kinetic energy (MIKE) spectrometry. High-resolution accurate mass data provide necessary confirmatory evidence for the proposed fragmentation mechanisms. In this paper only the mass spectrometric behaviour and proposed fragmentation mechanisms of the new compounds are reported. Information relating to the method of synthesis has been discussed elsewhere.<sup>5</sup>

## Experimental

The six new compounds were synthesized<sup>5</sup> in our laboratory. Reagents and solvents were purified in usual way. The crude products were purified by recrystallization or chromatography. All the six new compounds are solid at room temperature.

\* E-mail: myhe@chem.pku.edu.cn

Received December 10, 2001; revised February 8, 2002; accepted April 11, 2002.

Project supported by the National Natural Science Foundation of China (Nos. 29972002 and 20075002).

Elemental analysis was performed using a Vario EL (Elementar, FRG); IR spectra were obtained using a FT-750 IR spectrophotometer (Nicolet, USA). Nuclear magnetic resonance spectra ( $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR) were measured using an ARX 400 spectrometer (Bruker, Fällanden, Switzerland). All mass spectral data were obtained using a double-focusing mass spectrometer ZAB-HS (Micromass, Manchester, UK) coupled with a MASPEC II data system. The electron impact (EI) source temperature was 200 °C, and compounds were introduced into the mass spectrometer by direct insertion probe using a probe temperature ramp from 30 °C to 150 °C, 180 °C or 200 °C. The ionizing energy was 70 eV. High-resolution accurate mass data for some of the ions were also obtained using the same instrument with a resolution of 5000 (10% valley) by the peak matching technique with perfluorokerosene (PFK) as a reference compound. The accurate masses of some ions were obtained using a FTMS APEX 4.7-T mass spectrometer (Bruker Instruments, Billerica, MA USA). Unimolecular MIKE spectra were obtained under the control of the MASPEC II data system.

## Results and discussion

The structures of the six new compounds are similar, but there are differences between them, so that the MS fragmentation pathways of the six compounds not only are alike, but also exhibit interesting differences.

The EI spectra of the six compounds are listed in Table 1, showing the very intense molecular ion peaks  $\text{M}^+$  (44%—100%). The relative abundances of frag-

ment ions **a—o** are all significant. An ion at  $m/z$  29 and aromatic series ions at  $m/z$  39, 51, 65, 77, 91 *etc.*, were observed for each compound.

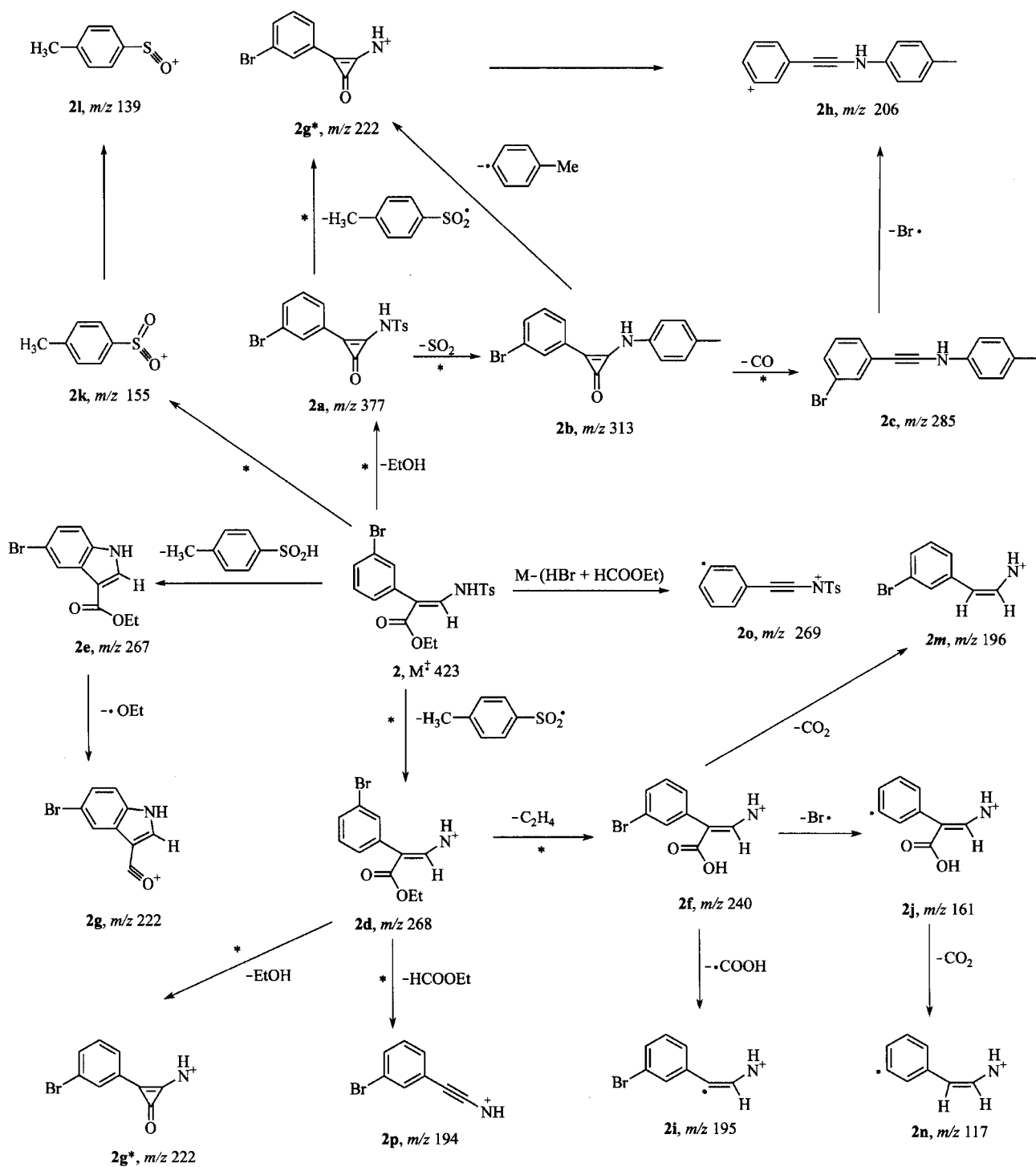
The mass spectrometric fragmentation pathways of compounds **1**, **2**, **3**, **4** and **6** are very similar. We take the compound **2** as an example to describe these fragmentations. The EI spectrum of compound **2** is shown in Fig. 1, and the fragmentation pathways in Scheme 2. The molecular ion  $\text{M}^+$  produces the odd-electron ion **2a** ( $\text{OE}^+$ ) by losing a neutral molecule of EtOH; the MIKE spectra showed that the ion **2b** at  $m/z$  313 originates from ion **2a** at  $m/z$  377. From high-resolution mass data (Table 2), the  $m/z$  value of ion **2b** is 313.01066, which corresponds accurately to the elemental composition of  $\text{C}_{16}\text{H}_{12}\text{NO}^{79}\text{Br}$ , thus supporting the interpretation that the odd electron ion **2b** ( $\text{OE}^+$ ) is formed through a skeletal rearrangement<sup>7,8</sup> as ion **2a** expels  $\text{SO}_2$ . At  $m/z$  313 in Fig. 1 there is also a Br isotope peak at  $m/z$  315; ion **2b** in turn becomes the odd electron ion **2c** ( $\text{OE}^+$ ) by losing CO. The  $\text{M}^+$  yields the  $\text{EE}^+$  ion **2d** by expelling the radical  $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\cdot$  through *i*-cleavage. In a parallel process, molecular ion forms a new five-membered ring<sup>9,10</sup> by expelling the neutral molecule  $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{H}$  to form the odd electron ion **2e** ( $\text{OE}^+$ ). Ion **2f** can be obtained when ion **2d** loses ethene, possibly via a McLafferty rearrangement.<sup>11</sup> Ion **2g** ( $m/z$  222) is generated as ion **2e** expels the radical group  $\text{EtO}\cdot$ . Ions at  $m/z$  222 can also be produced via ions **2a**, **2b** and **2d**, although no MIKES peak was recorded for the **2b** reaction. As the structures of the above ions at  $m/z$  222 are

Table 1 EI-MS of compounds **1—6**:  $m/z$  (RA) data

No.	$\text{M}^+$	a	b	c	d	e	f	g	$\text{g}^+$	h	i	j	k	l	m	n	o	Other ions	
1	345	299	235	207	190	189	162	144	144	206	117	161	155	139	118	117	190		
	100.0	47.1	29.3	8.1	4.5	5.01	12.9	74.1	74.1	2.5	54.1	4.5	17.9	22.8	90.4	54.0	4.5		
2	423	377	313	285	268	267	240	222	222	206	195	161	155	139	196	117	269	91	
	44.5	20.4	5.8	2.6	3.0	5.0	2.9	20.4	20.4	7.9	41.8	23.6	26.0	26.0	6.1	41.8	7.8	100.0	
3	379	333	269	241	224	223	196	178	178	/	151	/	155	139	152	/	/	117	91
	66.5	13.3	6.7	3.3	2.1	3.5	7.3	27.1	27.1	/	33.0	/	20.3	29.9	38.8	/	/	35.2	100
4	375	329	265	237	220	219	192	174	174	206	147	161	155	139	148	117	221		
	70.3	30.8	18.2	2.1	13.8	3.4	22.4	43.4	43.4	0.9	100	4.5	6.7	11.1	96.4	14.2	3.2		
5 <sup>a</sup>	359	313	204	188	158	155	130											91	
	82.2	18.5	17.4	10.9	61.8	18.7	93.6											100	
6	405	359	295	267	250	249	222	204	204	/	177	191	155	139	178	147	251	221	360, 205
	69.2	5.4	1.9	1.8	38.0	6.3	10.7	100.0	100.0	/	39.2	3.1	10.1	9.4	34.0	12.6	27.8	12.8	5.1, 41.5

<sup>a</sup> The meaning of ions **b—f** of compound **5**, please see Scheme 3.

**Scheme 2** Fragmentation pathways proposed for compound **2** (the fragmentation pathway marked with an asterisk were observed in MIKES experiments).

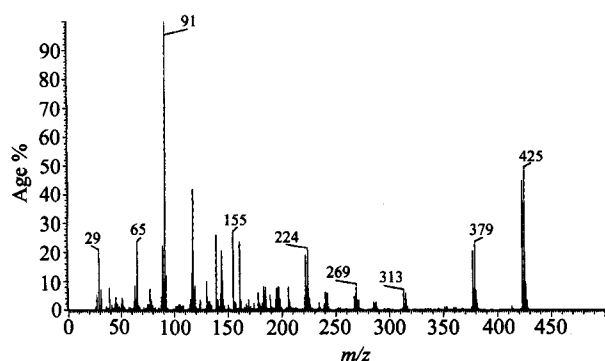


proposed to be different from that of ion **2g**, they are therefore marked as **2g\*** in Scheme 2. However, the elemental compositions of **2g** and **2g\*** are entirely the same,

since only one single peak could be observed in the high resolution experiment.

**Table 2** High-resolution accurate mass data of compound **2**

$m/z$	Measured value	Calculated value	Difference ( $\mu$ )	Elemental composition
423	423.0123	423.0140	-1.7	C <sub>18</sub> H <sub>18</sub> NO <sub>4</sub> BrS
377	376.9720	376.9721	-0.1	C <sub>16</sub> H <sub>12</sub> NO <sub>3</sub> BrS
313	313.0107	313.0102	+0.5	C <sub>16</sub> H <sub>12</sub> NOBr
285	285.0147	285.0153	-0.6	C <sub>15</sub> H <sub>12</sub> NBr
269	269.0515	269.0511	+0.4	C <sub>15</sub> H <sub>11</sub> NO <sub>2</sub> S
268	267.9979	267.9973	+0.6	C <sub>11</sub> H <sub>11</sub> NO <sub>2</sub> Br
267	266.9907	266.9895	+1.2	C <sub>11</sub> H <sub>10</sub> NO <sub>2</sub> Br
240	239.9653	239.9660	-0.7	C <sub>9</sub> H <sub>7</sub> NO <sub>2</sub> Br
222	221.9554	221.9555	-0.1	C <sub>9</sub> H <sub>5</sub> NOBr
206	206.0959	206.0970	-1.0	C <sub>15</sub> H <sub>12</sub> N
195	194.9679	194.9684	-0.5	C <sub>8</sub> H <sub>6</sub> NBr
161	161.0474	161.0477	-0.3	C <sub>9</sub> H <sub>7</sub> NO <sub>2</sub>
155	155.0162	155.0167	-0.6	C <sub>7</sub> H <sub>7</sub> O <sub>2</sub> S
139	139.0215	139.0218	-0.3	C <sub>7</sub> H <sub>7</sub> OS
196	195.9761	195.9762	-0.1	C <sub>8</sub> H <sub>7</sub> NBr
117	117.0580	117.0579	-0.1	C <sub>8</sub> H <sub>7</sub> N

**Fig. 1** EI-MS of Compound **2**.

Ion **2c** ( $m/z$  285) of compound **2** produces ion **2h** ( $m/z$  206) by losing the Br $\cdot$  atom, as confirmed from the isotope patterns (Fig. 1). Ion **2i** is obtained when ion **2f** loses the COOH $\cdot$  radical. Ion **2j** is formed by losing the Br $\cdot$  from ion **2f**, as confirmed from the isotope patterns (Fig. 1). The molecular ion yields ion **2k** through  $\alpha$ -cleavage by radical-site initiation. Ion **2k** produces ion **2l** by losing one oxygen atom. Ion **2f** produces ion **2m** by losing CO<sub>2</sub>. Ion **2o** is formed when the molecular ion M<sup>+</sup> loses (HBr + HCOOEt). Compounds **1**, **2**, **3**, **4** and **6**, except those ions marked with "\*" in Table 1, will produce ions **a—o** following the above-mentioned similar pathways. In addition, an ion at  $m/z$  117 from compound **3** is formed by losing Cl $\cdot$  from ion **m**. The peak matching method was used to measure accurately masses data for most important ions of compound **2** (Table 2),

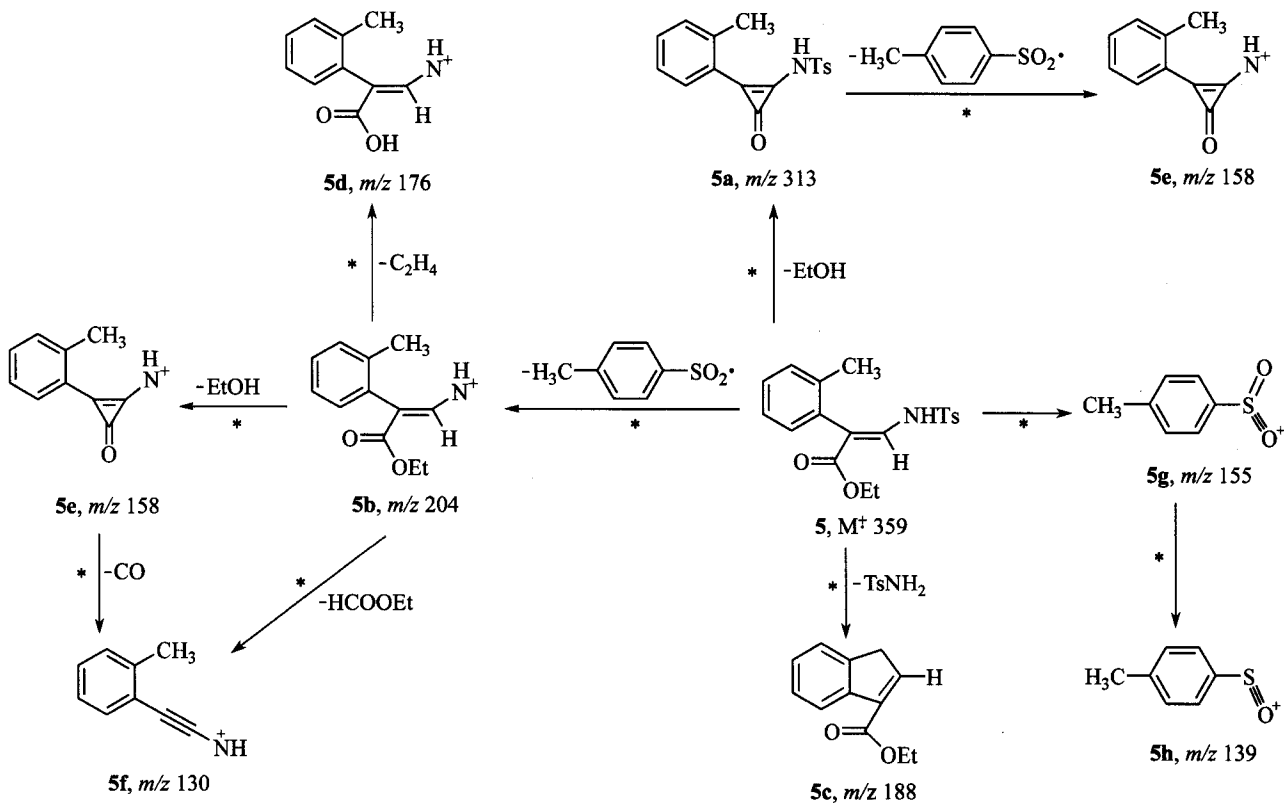
and the unimolecular spectra MIKES of some ions were also obtained (Table 3). All these data support the proposed fragmentation pathways.

**Table 3** MIKE Spectra of ions derived from compounds **2** and **5**

No.	Parents ions	Daughter ions
<b>2</b>	423	377, 268, 155
	377	313, 222
	313	285
	268	240, 222, 194
<b>5</b>	359	313, 204, 188, 155
	313	158
	204	176, 158, 130
	158	130

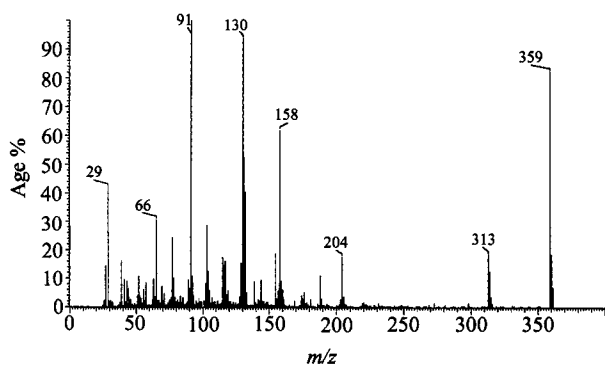
For compound **5**, with a CH<sub>3</sub>-substituted group in the *ortho*-position (*o*-Me) of the benzene ring, the fragmentation pathway showed the characteristic evidence for an *ortho*-effect. The EI mass spectrum and proposed fragmentation pathways of compound **5** are shown in Fig. 2 and Scheme 3, respectively. Scheme 3 shows that most fragmentation processes are the same as those of the above-mentioned five compounds. There is only one unique fragmentation process of compound **5**, which involves formation of a new five-membered ring by loss of a TsNH<sub>2</sub> group from the molecular ion M<sup>+</sup> through a reaction involving an *ortho*-effect. This new ion is marked as ion **5c** ( $m/z$  188). Its measured accurate mass value is

**Scheme 3** Fragmentation pathways proposed for compound **5** (the fragmentation pathway marked with an asterisk were observed in MIKES experiments).



**Table 4** The accurate mass data of compound **5** in high-resolution

<i>m/z</i>	Measured value	Calculated value	Difference ( <i>mu</i> )	Elemental composition
359	359.11898	359.11913	-0.15	C <sub>19</sub> H <sub>21</sub> NO <sub>4</sub> S
313	313.07748	313.07727	+0.2	C <sub>17</sub> H <sub>15</sub> NO <sub>3</sub> S
204	204.10130	204.10245	-1.2	C <sub>12</sub> H <sub>14</sub> NO <sub>2</sub>
188	188.08277	188.08373	-0.9	C <sub>12</sub> H <sub>12</sub> O <sub>2</sub>
176	176.07103	176.07115	-0.1	C <sub>10</sub> H <sub>10</sub> NO <sub>2</sub>
158	158.05987	158.06059	-0.7	C <sub>10</sub> H <sub>8</sub> NO <sub>2</sub>
155	155.01659	155.01668	-0.1	C <sub>7</sub> H <sub>7</sub> O <sub>2</sub> S
139	139.02158	139.02176	-0.2	C <sub>7</sub> H <sub>7</sub> OS
130	130.06534	130.06567	-0.3	C <sub>9</sub> H <sub>8</sub> N



**Fig. 2** EI-MS of Compound **5**.

188.0828, differing by only 0.9 *mmu* from the calculated value 188.0837 for the elemental composition C<sub>12</sub>H<sub>12</sub>O<sub>2</sub> (Table 4). Based on the MIKES spectrum of M<sup>+</sup> at *m/z* 359, ion **5c** arises from the molecular ion M<sup>+</sup> (Table 3), which supports the proposed mechanism involving an ortho effect.

## Conclusion

All six new compounds investigated here possess obvious characteristic fragmentations under EI conditions.

Each compound shows the very intense molecular ion peak, and produces the odd electron ion  $M^{\ddagger} - \text{MeOH}$ , the even electron ion  $[M - (\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\cdot)]^+$ , and the  $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2^+$  ion, etc.. A McLafferty rearrangement reaction of the ester group is also observed. In addition, various fragmentation pathways occur with the changes of the substitution of the aromatic rings. For compound **5**, it has an *ortho*-methyl substituent, a cyclization reaction with loss of neutral  $\text{TsNH}_2$  to yield an odd electron ion (Scheme 3, **5c**) with a new five-membered ring was observed. For compounds **2**, **3**, **4** and **6** with *meta*- and *para*-substitution, ions formed by skeletal rearrangement reactions (Scheme 2, ion **b**) are observed. The above conclusions are consistent with the results of MIKE spectrometry and of precise mass measurements in high resolution.

## References

- 1 Doyle, M. P.; Mckervery, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*, Wiley-Interscience, New York, 1998.
- 2 Newman, M. S.; Beal, P. E. *J. Am. Chem. Soc.* **1950**, *72*, 5163.
- 3 Iketa, N.; Takamura, N.; Ganem B. *Tetrahedron Lett.* **1981**, *22*, 4163.
- 4 Ye, T.; Mckervery, M. A. *Tetrahedron* **1992**, *48*, 8007.
- 5 Jiang, N.; Qu, Z.; Wang, J. *Org. Lett.* **2001**, *3*, 2889.
- 6 (a) Cimarelli, C.; Palmieri, G. *J. Org. Chem.* **1996**, *61*, 5557.  
(b) Zhu, G.; Chen, Z.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 6907.
- 7 He, M. Y.; Ye, Y. H.; He, X. R.; Huang, Y. S.; Lin, X. Y.; Yu, Z. P. *Org. Mass Spectrom.* **1992**, *27*, 636.
- 8 Yu, Z. P.; Yuan, J. F.; Lin, X. Y.; He, M. Y.; Zhang, M. Z. *Org. Mass Spectrom.* **1989**, *24*, 283.
- 9 Schubert, R.; Grützmacher, H. F. *Org. Mass Spectrom.* **1980**, *15*, 122.
- 10 He, M. Y.; Yu, Z. P.; Hua, W. T. *Org. Mass Spectrom.* **1989**, *24*, 271.
- 11 McLafferty, F. W.; Turecek, F. *Interpretation of Mass Spectra*, 4th ed., University Science Books, Sausalito, California, **1993**, p. 72.

(E0112101 LU, Y. J.; LING, J.)